

Remarks

The Office Action mailed January 7, 2003 has been received and reviewed. Claims 1-30 and 44-46 having been canceled, claim 42 having been amended, and claim 49 having been added, the pending claims are claims 31-43 and 47-48. Of the pending claims, claims 38-43 are currently under examination, with claims 31-37 and 47-48 having been withdrawn from consideration. Reconsideration and withdrawal of the rejections are respectfully requested.

The specification has been amended at page 7, line 18; page 16, line 30; page 24, line 10; and page 49, line 3 to correct typographical errors. The specification has also been amended at page 26, line 10 to clarify that Applicants have not recited an embedded hyperlink.

Claim 42 has been amended to correct a typographical and grammatical errors.

New claim 49 has been added to recite a "[c]rystalline Hepatitis C virus helicase wherein the amino acid sequence of Hepatitis C virus helicase is SEQ ID NO:1," which is supported, for example, by originally filed claim 42.

Objection to the Specification

The Examiner objected to the specification because of formalities (e.g., misspellings). Applicants respectfully submit that the amendments to the specification (e.g., page 7, line 18; page 16, line 30; page 24, line 10; and page 49, line 3) to correct typographical errors renders the objection moot.

The Examiner also objected to the specification as allegedly containing an embedded hyperlink. Applicants respectfully submit that the amendment to the specification (e.g., page 26, line 10) to clarify that Applicants have not recited a hyperlink renders the objection moot.

Applicants respectfully request that the Examiner reconsider and withdraw the objections to the specification.

Objection to the Claims

The Examiner objected to claim 42 because of a formality (e.g., awkward grammatical structure). Applicants respectfully submit that the amendment to claim 42 to correct typographical and grammatical error renders the objection moot. Applicants respectfully request that the Examiner reconsider and withdraw the objection to the claims.

Rejections under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 39, 41, and 43 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleged that claims 39 and 41 are vague and indefinite because it is not clear whether the sequence is referring to the entire sequence or just a fragment of the sequence. Applicants respectfully traverse the rejection.

Applicants respectfully submit that the claims clearly and distinctly convey the claimed invention to one of skill in the art. Specifically, claims 39 and 41 both recite that "the amino acid sequence of Hepatitis C virus helicase *is* SEQ ID NO:1" (emphasis added). Nowhere in claims 39 and 41 is there any language that would lead one of skill in the art to interpret the recitations as referring to a "fragment." Thus, the Examiner's assertion that the sequence might refer to a fragment is totally unsupported. Applicants respectfully submit that the recitations of claims 39 and 41 clearly and distinctly convey to one of skill in the art that the entire amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.

The Examiner also rejected claim 42 as being dependent on claims 39 and 41. Applicants respectfully request clarification of this rejection in the next Official Communication, as claim 42 is an independent claim. In the event that the Examiner was instead referring to claim 43, then Applicants respectfully submit that the rejection is obviated in light of the remarks presented herein above in regard to claims 39 and 41, from which claim 43 depends.

Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §112, second paragraph.

Rejections under 35 U.S.C. §112, First Paragraph

Rejection for Lack of Enablement

The Examiner rejected claims 42 and 43 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner acknowledged that the specification provides enablement for making crystals of crystalline Hepatitis C virus helicase with unit cell dimensions of $a = b = 109 \text{ \AA} \pm 3 \text{ \AA}$; $c = 84 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P4_1$; as well as $a = 66 \text{ \AA} \pm 2 \text{ \AA}$; $b = 110 \text{ \AA} \pm 3 \text{ \AA}$; $c = 64 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and a space group $P2_12_12_1$; but alleged that the specification does not reasonably provide enablement for other crystalline Hepatitis C virus helicases and compositions including the same. Applicants respectfully traverse the rejection.

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P. §2164.04. "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." M.P.E.P. §2164.01(b). "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be *used* in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not *use* the genus as a whole without undue experimentation." M.P.E.P. §2164.02, paragraph entitled "WORKING EXAMPLES AND A CLAIMED GENUS" (emphasis added). "[E]ven in unpredictable arts, a

disclosure of every operable species is not required." M.P.E.P. §2164.03.

The specification clearly defines the protein to be crystallized as being Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1 (e.g., Figure 2 and claims 37, 39, and 41-42). The specification clearly describes methods of crystallizing Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1 (e.g., page 11, line 21 to page 12, line 12, and claims 31 and 35). Although not required, and as admitted by the Examiner, Applicants have even provided working examples of making two different crystals (e.g., having different space groups and different cell dimensions) of Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1 (e.g., page 39, line 28 to page 41, line 7). Further, the specification provides methods of using crystals of Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1 including, for example solving crystal structures (e.g., pages 12-17) and incorporating a chemical entity in a crystal (e.g., claims 47-48). Notably, the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification.

In spite of the disclosure provided in the specification as noted above, the Examiner asserted that "the specification does not reasonably provide enablement for other crystalline Hepatitis C virus helicases and compositions comprising the same." Applicants respectfully reiterate that, as quoted from the M.P.E.P. herein above, *a disclosure of every operable species is not required*. Applicants respectfully submit that one of skill in the art, using the disclosure provided in the specification (including the working examples), would be able to make and use the entire scope of the invention as recited in claim 42. For example, Applicants' disclosure of methods of making and using two different crystals of Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1 may provide tools for one of skill in the art, without undue experimentation, to make additional crystals of Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1. For example, one of skill in the art might use the presently disclosed crystals in, for example, cross-seeding techniques (*see* the specification at, for example, page 39, line 29, and page 40, lines 2 and 23-24, for disclosure of seeding) to make additional crystals of Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1.

Moreover, the specification discloses working examples of compositions including crystalline Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1 (e.g., claim 43). In addition to Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1, the disclosed compositions include, for example, water, dimethyl sulfoxide, glycerol, polyethylene glycols, polyethylene glycol monoethers, salts, buffers, and combinations thereof (e.g., crystals in cryogenic solutions as described, for example, in the specification at page 40, lines 25-26; page 41, lines 8-17 and 26-28). Notably, Applicants are not claiming co-crystals or liganded complexes (e.g., claims 38-43), and the claimed compositions do not require chemical entities or ligands as suggested by the Examiner.

Thus, Applicants respectfully submit that claims 42 and 43 are fully enabled by the specification.

Rejection for Lack of Written Description

The Examiner rejected claims 38-43 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

First, regarding claims 38, 40, and 43 (and dependent claims 39 and 41), the Examiner noted that open claim language is used (e.g., "comprising" and "having") such that the crystalline Hepatitis C virus helicase might include other crystals which do not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicants respectfully traverse the rejection.

Applicants agree that claims 38, 40, and 43 use open claim language, which means that the crystalline Hepatitis C virus helicase must include the subject matter described in the claim, and may optionally include additional subject matter (e.g., other crystals). The Examiner has not provided any convincing reasons or rationale as to why the subject matter described in the claims does not meet the written description provision of 35 U.S.C. §112, first paragraph, but instead has chosen to focus on *lack of written description for what is not recited*

in the claims. Thus, Applicants respectfully submit that the rejection is not a written description rejection to the subject matter described in the claims, but a rejection to the use of "comprising" and "having" as transitional phrases. Applicants respectfully traverse the rejection and submit that the use of "comprising" or "having" as a transitional phrase is proper and is even acknowledged by the M.P.E.P. (*see, for example*, M.P.E.P. §2111.03).

Second, regarding claims 39 and 41-42 (and dependent claim 43), the Examiner asserted that the amino acid sequence may contain the entire sequence or "just a fragment of the sequence." Applicants respectfully disagree.

Claims 39 and 41 clearly recite that "the amino acid sequence of Hepatitis C virus helicase *is* SEQ ID NO:1" (emphasis added). Nowhere in claims 39 and 41 is there any language that would lead one of skill in the art to interpret the recitations as referring to a "fragment." Thus, the Examiner's assertion that the sequence might refer to a fragment is totally unsupported. Applicants respectfully submit that the recitations of claims 39 and 41 clearly and distinctly convey to one of skill in the art that the entire amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.

Claim 42, as amended, recites "[c]rystalline Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1." Nowhere in claim 42, either as originally filed or as amended, is there any language that would lead one of skill in the art to interpret the recitation as referring to a "fragment." Thus, the Examiner's assertion that the sequence might refer to a fragment is totally unsupported. Applicants respectfully submit that the recitation of claim 42 clearly and distinctly conveys to one of skill in the art that the Hepatitis C virus helicase includes the entire amino acid sequence SEQ ID NO:1.

Based on the remarks presented herein above, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §102

The Examiner rejected claims 42 and 43 under 35 U.S.C. §102(b) as allegedly being anticipated by Kim et al. ("Hepatitis C Virus NS3 RNA Helicase Domain with a Bound

Oligonucleotide: The Crystal Structure Provides Insights into the Mode of Unwinding," *Structure*. 1998;6(1):89-100). Specifically, the Examiner alleged that Kim et al. disclose a crystalline Hepatitis C virus helicase with an amino acid sequence (Figure 5) (amino acid residues 1359-1474) that identically matches a *fragment* of SEQ ID NO:1 (amino acid residues 168-283). Applicants respectfully traverse the rejection.

Claim 42, as amended, recites "[c]rystalline Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1," and claim 43 depends from claim 42. Nowhere in claim 42, either as originally filed or as amended, is there any language that would lead one of skill in the art to interpret the recitation as referring to a "fragment." Thus, the Examiner's assertion that the sequence might refer to a fragment is totally unsupported. Applicants respectfully submit that the recitation of claim 42 clearly and distinctly conveys to one of skill in the art that the Hepatitis C virus helicase includes the entire amino acid sequence SEQ ID NO:1.

Kim et al. fails to disclose or suggest, among other things, a crystalline Hepatitis C virus helicase that includes the entire amino acid sequence SEQ ID NO:1. Moreover, even the *fragment* of Kim et al. noted by the Examiner (i.e., amino acid residues 1359-1474) fails to disclose or suggest the *fragment* of SEQ ID NO:1 cited by the Examiner (i.e., amino acid residues 168-283). Applicants respectfully note that the alignment kindly supplied by the Examiner shows that the fragments differ, for example, at residues 245 and 253 of SEQ ID NO:1 (i.e., A and Y), which were aligned with residues 1436 and 1444 of Kim et al. (i.e., S and F).

Thus, Applicants respectfully submit that claims 42 and 43 are not anticipated by Kim et al. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102.

New Claim

New claim 49 has been added to recite a "[c]rystalline Hepatitis C virus helicase wherein the amino acid sequence of Hepatitis C virus helicase is SEQ ID NO:1." Applicants respectfully submit that new claim 49 is patentable for reasons similar to those presented herein above for the patentability of claims 38-43.

Request for Rejoinder of Claims Withdrawn from Consideration

Claims 31-37 recite methods for making crystalline Hepatitis C virus helicase (e.g., crystallizing or co-crystallizing a Hepatitis C virus helicase molecule or molecular complex). Claims 47-48 recite methods of using crystalline Hepatitis C virus helicase (e.g., incorporating a chemical entity in a crystal). Upon allowance of any of the elected product claims, rejoinder of the non-elected method claims is respectfully requested pursuant to M.P.E.P. §821.04. *See, also, In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996).

Information Disclosure Statement

Applicants thank the Examiner for initialing and returning a copy of the 1449 form submitted with an Information Disclosure Statement mailed November 7, 2002.

The Examiner also indicated that the Information Disclosure Statement mailed January 11, 2002 failed to comply with 37 C.F.R. §1.98(a)(2), as the Information Disclosure Statement allegedly did not include a legible copy of each of the documents listed on the 1449 forms. Applicants respectfully submit that copies of each of the documents (55 total) listed on the five 1449 forms were mailed with the Information Disclosure Statement on January 11, 2002, as confirmed by the postcard which was stamped as received by the United States Patent and Trademark Office and returned to Applicants' Representatives (Exhibit A). Thus, Applicants respectfully submit that the Information Disclosure Statement was in compliance with 37 C.F.R. §1.98(a)(2), and respectfully request that the documents listed on the 1449 forms be considered during examination on the merits.

Applicants Representatives are aware that documents sometimes do become separated in the Patent Office from the Information Disclosure Statements with which they were submitted. As a courtesy, Applicants are submitting herewith courtesy copies of the previously submitted documents and clean copies of the 1449 forms (Exhibit B).

Consideration of each of the documents listed on the attached 1449 form(s) is respectfully requested. Pursuant to the provisions of M.P.E.P. §609, Applicants further request

Amendment and Response

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For: HEPATITIS C VIRUS HELICASE CRYSTALS, CRYSTALLOGRAPHIC STRUCTURE AND METHODS

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that a copy of the 1449 form(s), marked as being considered and initialed by the Examiner, be returned with the next Official Communication

Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
Finzel et al.

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PATENT TRADEMARK OFFICE

May 7, 2003
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CERTIFICATE UNDER 37 CFR §1.10:

"Express Mail" mailing label number: **EV 183608275 US**

Date of Deposit: **MAY 7, 2003**

The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: [Signature]
Name: **SAM HER**